1. **Equine Ocular Squamous Cell Carcinoma**

2. **Equine Ocular Emergencies**

3. **Diagnostic Approach to the Cloudy Eye: What to Do If the Eye Is Blue (or White or Yellow)**

4. **Ocular Prepurchase Examination: No Eye, No Horse**
1. Equine Ocular Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) is the most common periocular tumor reported in horses. The clinical presentation of SCC is often raised, pink, rough, and irregular, with the prototypical SCC having been described as “pink cauliflower”.

SCC occurs in one of three periocular locations: eyelid, nictitans (third eyelid, TE), and limbus (junction of cornea and sclera), each of which may manifest in a range of clinical presentations and each of which has its own list of recommended therapies.

SCC is an epithelial tumor, and as such, tends to be locally aggressive, but metastatic disease is possible. Of the three locations, limbal SCC is most likely to be associated with loss of the globe, but TE SCC, ironically because it is the easier to remove under only standing sedation, is most likely to be associated with terminal disease, when tumor cells migrate into the orbit, invade bone or involve the brain.

Risk factors for development of SCC include solar radiation, light coat, and breed, with Paints, Appaloosas, Belgians and Haflingers overrepresented. Coat color and breed risk factors may be confounded. SCC does tend to be a cancer of older horses, but as with other forms of cancer, horses of any age may be affected.

The roles of gross and histologic features such as tumor size, high mitotic index and lymphatic invasion have not been well clarified in terms of likelihood of disease resolution after surgical excision.

Pathophysiology

Ultraviolet light has been implicated in the development of SCC, by causing mutations in a tumor suppressor gene, p53. Additionally, cyclooxygenase derived prostaglandins, specifically COX-2, may be upregulated in association with p53 mutations, stimulating tumor growth, metastasis and angiogenesis.

Therapy

Numerous therapies exist for SCC, as with any disease for which there is no perfect treatment. The choice of therapy may not be as critical as early intervention. Excision is often combined with an adjunctive therapy. Excision of SCC involving the nictitans can typically be performed standing, if the tumor is focal and complete excision can be accomplished.
Cryoablation is typically used for lesions <2mm in thickness. Optimal cryonecrosis is achieved between -20C and -40C, using a double freeze thaw technique. A fast freeze and slow thaw facilitates cryodestruction. Cryotherapy has the advantages of being accessible and portable. Adverse effects are uncommon, although excessive granulation tissue can be associated with cryotherapy for limbal tumors. Cryotherapy can be used for lid, nictitans, and limbal SCC (Bosch & Klein, 2005).

5-fluorouracil is a pyrimidine analog that acts as an antimetabolite, by noncompetitive inhibition of thymidylate synthase. It can be used topically for limbal SCC, and intralesionally for lid SCC.

Mitomycin-C is an aziridine-containing natural product isolated from Streptomyces species. It acts as a potent DNA crosslinker. Its use topically is based on a retrospective study of 10 human patients with extensive recurrent limbal SCC (Shields et al., 2002). Topical use in horses has been shown to be effective (Clode et al., 2012).

Photodynamic therapy (PDT) involves the use of photochemical reactions mediated through the interaction of photosensitizing agents, light and oxygen. Tumor tissue is injected with verteporfin, and laser radiation is applied. This induces oxidative damage to the microvasculature, contributing to ischemic tumor death (Giuliano, 2008).
Radiation has been used as primary and adjunctive therapy to treat SCC. Strontium 90 (Sr90) penetrates to a depth of approximately 3mm, with 80% of the radiation dose absorbed in the first 2mm, and thus may be effective for limbal SCC (Plummer et al., 2007). Iridium 129 (Ir129) is delivered via implants for eyelid SCC. Cobalt 60 (Co60) is associated with deeper penetration and thus does not have periocular application, due to risks of collateral damage.

Cisplatin is a platinum based chemotherapy drug that binds to and causes crosslinking of DNA, which triggers apoptosis of tumor cells. It is most commonly used intralesionally, in conjunction with surgical excision. Cisplatin-containing biodegradable beads have been used to treat cutaneous SCC (Hewes & Sullins, 2006), but these can cause adverse effects on the cornea associated with high local concentrations of the drug.

REFERENCES


Many equine ocular emergencies have as an initial complaint a “swollen eye” – blepharedema, blepharitis, ocular discharge, conjunctival hyperemia, and corneal edema. These signs can represent a host of ocular conditions. The most common equine ocular emergencies include lid lacerations, melting ulcers, iris prolapse (either traumatic or ulcerative), blunt trauma, orbital fracture, severe uveitis, and glaucoma.

**EMERGENCY OCULAR EXAMINATION**

It is tempting in an emergency situation to jump right to the complaint (e.g., iris prolapse – yep, there’s brown in the cornea!) but don’t skimp on doing a complete eye examination as important information can be missed (e.g., was there an indirect PLR from the eye with the iris prolapse to the contralateral eye?) that might help with decision making regarding the disposition of the eye (e.g., if there’s an indirect PLR, maybe vision could be retained). Adequate sedation and restraint are critical for the safety of the examiner, the handler, and the horse, as well as to prevent any damage to the globe that might result from a struggle with the horse to get a look at the eye. As a part of a complete eye exam, fluorescein sodium should be directly instilled into the eye to assess the integrity of the corneal epithelium. This can be performed by placing a drop of eyewash onto the fluorescein strip and then touching it gently to the conjunctiva or by placing the fluorescein strip in a 3cc syringe and then filling it with 0.2-0.3mL of eyewash or sterile saline. A 25g needle can be placed on the syringe and the needle cap used to gently break the needle from the hub, creating a convenient device for squirting the fluorescein solution onto the ocular surface. Excess fluorescein should be rinsed away with sterile saline or eyewash to prevent pooling of the stain and false positive results.

**Auriculopalpebral nerve block.** Ocular examination of a horse with a painful eye, or one that is fragile enough to raise concerns about globe rupture with pressure on the lids, can be facilitated by performing an auriculopalpebral nerve block. This block provides akinesia of the orbicularis oculi muscle, which is responsible for eyelid closure, but eyelid sensation persists. In addition, this block may be useful for diagnostic procedures including corneal culture and cytology, as well as for placement of subpalpebral lavage systems and any other procedure in which a firmly closed lid would be prohibitive.

The auriculopalpebral is a branch of the facial nerve. Its palpebral branch can be palpated in two places, just lateral to the dorsal-most border of the zygomatic arch, and on the zygomatic arch caudal to the bony process of the frontal bone. Injection of 1 to 1.5mL of 2% lidocaine hydrochloride at either of these sites should result in paralysis of the superior lid within several minutes, and this paralysis may last several hours. Corneal dessication typically does not result from this temporary inability to blink due to resultant ptosis. In addition to these two sites, the palpebral nerve may be blocked just anterior to the base of the ear, although it cannot be palpated at this site. Two-percent mepivicaine may be used instead of lidocaine; it has a similar onset and slightly longer duration of action.
To perform the auriculopalpebral block, a 25-gauge needle without a syringe attached is gently pushed through the skin adjacent to the nerve. The needle is held in one hand and the skin tented with the opposite hand to facilitate needle placement. Placement of the needle typically elicits head tossing and thus one must be careful not to inadvertently stab another site on the horse or oneself, or drop the needle, if this occurs. Prior to performing the block, clearing the floor of bedding directly in front of the horse, or moving the horse to an area where a dropped needle may easily be located, may save time and frustration should the needle wind up on the ground instead of in the horse’s head. Once the needle is positioned through the skin, the hub should be grasped with the opposite hand to prevent movement of the needle under the skin, and a non-Luer lock 3mL syringe containing the anesthetic should be attached, and the anesthetic injected. If the anesthetic proves difficult to inject, even blowing the syringe backwards off the needle and spraying anesthetic (possibly in one’s face), the needle has most likely been placed intradermally and should be redirected deeper so that it is truly subcutaneous. Repeatedly redirecting the needle while injecting (which is sometimes done to facilitate diffusion of the anesthetic) is not recommended, as this practice could lead to breaking the needle off subcutaneously if the horse jerks the head. Once the anesthetic has been injected, the needle and syringe should be withdrawn together. There is typically no need to massage the injection site to achieve a good auriculopalpebral block.

Lidocaine is acidic and is reported by humans receiving a skin block to briefly burn on injection. Studies with humans show that buffering lidocaine with sodium bicarbonate to achieve a solution with a more physiologic pH results in less pain on injection without a loss of anesthetic effect. Buffered lidocaine is used in small animals for local blocks, but typically not in horses.

**Eyelid anesthesia.** Anesthesia of the eyelids can be achieved by blocking the appropriate sensory branch of the trigeminal. The frontal nerve innervates the nasal and central superior lid, and can be blocked at the supraorbital foramen, which can be palpated as a depression nasal to the narrowest aspect of the supraorbital process of the frontal bone. This is commonly called a supraorbital block, but it is called a frontal block as well. To perform the supraorbital block, a 25-gauge needle is injected into or just over the supraorbital foramen, and then 1 to 1.5mL of anesthetic injected. It is not necessary for the needle to enter the foramen to achieve a good block. The supraorbital block is most commonly used to anesthetize the superior lid prior to placement of a subpalpebral lavage. The temporal superior lid is innervated by the lacrimal nerve, which can be blocked along the temporal aspect of the orbital rim. The infratrochlear nerve innervates the nasal aspect of the inferior lid as well as the medial canthus, and it can be blocked at the palpable trochlear notch, on the medial aspect of the orbital rim. These three nerves (frontal, lacrimal, and infratrochlear) are branches of the ophthalmic branch of the trigeminal nerve. The temporal inferior lid is innervated by the zygomatic nerve, a branch of the maxillary branch of the trigeminal nerve. The zygomatic nerve can be blocked along the ventrolateral orbital rim. Depending on the intended site of placement of an inferior subpalpebral lavage, the zygomatic or infratrochlear nerve should be blocked.

**Corneal and conjunctival anesthesia.** Anesthesia of the cornea and conjunctiva (including palpebral and bulbar conjunctiva, as well as that overlying the nictitans) can be achieved by topical application of tetracaine or proparacaine. These topical anesthetics are most easily administered by drawing a small volume (0.5 to 1mL) into a syringe with a 25-gauge needle, breaking the needle off at the hub by rocking the needle back and forth several times within the
needle’s cap (partially placed over the needle to catch it as it falls off), and squirting the anesthetic onto the ocular surface. The nictitans can be anesthetized by injection of lidocaine or mepivicaine into its base, either through the inferior lid or directly into the nictitans after lowering the inferior lid to expose it. Duration of topical anesthesia using tetracaine or proparacaine has not been definitively established in the horse. For proparacaine, the maximal anesthetic effect occurs for about 5 minutes in cats and 15 minutes in dogs, and the duration of effect is about 25 minutes in the cat and 45 in the dog.

SUBPALPEBRAL LAVAGE CATHETERS

A subpalpebral lavage (SPL) catheter is a convenient method of delivering medications to the equine ocular surface. SPLs are useful when 1) the horse is difficult to treat, 2) the desired medication is a solution, 3) treatment will be long term, 4) the lids or cornea is very fragile or 5) the frequency of treatment is high. If placed incorrectly, however, corneal ulcers can result. One of the most common reasons for treatment failure amongst horses that are treated at home, and then referred to hospital, is inability to administer topical medication. If there is any question that topical medications can be successfully administered without an SPL, place one.

Commercial SPL kits are available through MILA. Two kits are available, the first with a 14-gauge needle and 18” tubing; the second with a 12-gauge needle and 36” tubing. The shorter tubing is often insufficient to reach the withers in a larger horse (e.g., warmblood or Thoroughbred with a long neck), and it can be difficult to reach the injection port to administer medications when the shorter tubing is used in a patient that elevates the head and neck in anticipation of treatment.

Upper or lower lid? The SPL may be placed either in the superior or inferior lid (Giuliano, 2000). Two factors contribute to the decision regarding which lid: location and character of the lesion, and temperament of the patient. First, placement of the SPL is recommended through the lid that exhibits the least blepharitis, and which overlies the...
smallest proportion of any corneal lesion. For example, an inferior lid SPL placement might be recommended in the case of a melting ulcer located in the superior cornea, just adjacent to the dorsal limbus, thereby avoiding surface contact with the ulcer of the gloved hand or the trochar used to insert the lavage through the lid. Second, temperament of the horse may contribute to a decision to place the SPL in the inferior lid, in patients for whom it would prove challenging to replace any of the butterfly sutures holding the SPL tubing in place on the face, should a suture break, due to difficulty handling or restraining such a patient. An example might be a foal that has not been frequently handled, is not halter-broken, and might be unduly stressed by re-suturing the tubing to the face. If the butterfly suture breaks in an inferior-lid SPL, there is no risk of the SPL footplate slipping and causing an SPL ulcer, as this would require footplate migration against gravity. If a suture breaks in a superior lid SPL, however, footplate migration onto the corneal surface can easily cause an ulcer that can be difficult to resolve.

Adequate sedation is mandatory to place an SPL. It is typical for a higher dose of sedative than is expected to be required to achieve adequate sedation due to most patients’ intense dislike of eyelid manipulation and of finger insertion between an eyelid and a painful cornea. Even a patient in five-point stance may toss the head skyward and react profoundly to insertion of even a finger under the eyelid, and this response must be avoided when inserting the large gauge trochar under the lid. Intravenous detomidine alone or in conjunction with torbugesic typically provides adequate sedation. Use of a nose twitch is recommended to guarantee adequate restraint, and thus to prevent inadvertent lid, conjunctival, or corneal laceration by the beveled end of the trochar, or injury to the veterinarian placing the SPL, should the patient toss the head while the trochar is being inserted through the lid.

**Nuts and bolts of SPL placement.** Start by performing an auriculopalpebral (motor) block, which is useful for an inferior SPL as well as a superior one, to paralyze the orbicularis muscle and thereby prevent strong blepharospasm from compromising access to the conjunctival fornix. Perform a frontal (also called supraorbital) (sensory) block to anesthetize the site through which the SPL trochar will pass. For a superior SPL, a supraorbital block is typically sufficient to provide anesthesia of the intended SPL trochar site. For an inferior SPL, however, a local block
using 1-1.5mL lidocaine is required. Then numb the cornea and conjunctiva with a topical anesthetic, and prepare the lid skin, cornea and conjunctival surface by squirting dilute betadine solution onto the lid in question and the ocular surface. This can be accomplished by drawing the 1:20 dilute Betadine solution into a 20mL syringe with a 25-gauge needle, and then breaking the needle off at the hub, allowing a fine stream of solution to be directed onto the lid, conjunctiva and cornea.

Test adequacy of sedation and local anesthesia by inserting a finger under the lid through which the SPL will be placed, and pushing down on that finger, through the lid, with a finger on the opposite hand. If the patient tolerates this, insertion of the SPL trochar will most likely be easily tolerated as well. Once the patient is adequately sedated and blocked, and the external lid and ocular surface is prepared with dilute betadine, open the SPL kit, ensure that the patient is restrained with a nose twitch, and don sterile gloves. Have an assistant hold the opened SPL kit ready, or place it within easy reach. Pick up the SPL trochar in the dominant hand, and use the opposite hand to open eyelids as needed to allow insertion of the SPL trochar, guided by the index finger, to the conjunctival fornix. It is mandatory that the trochar pass through the eyelid at the depth of the conjunctival fornix, no closer to the lid margin, to prevent footplate movement over the cornea and subsequent corneal ulceration. In a moment of truth, push the trochar through the skin, such that about half the needle has gone through the eyelid. This may require a strong push, with a feeling that periosteum has been penetrated.

With the non-dominant hand, guide the end of the SPL tubing through the length of the trochar, pull the trochar the remaining distance through the lid and off the tubing, and set the trochar down. Pull the tubing the remainder of the way through the eyelid. Place one butterfly about 25cm from the wound where the SPL tubing exits the skin, and place a single interrupted suture using 2-0 non-absorbable suture through the butterfly tape on either side of the tubing. Ensure that this butterfly is well-adhered to the tubing, so that the tubing does not slip toward the lid, dislodging the footplate. Place a second butterfly about 25cm down the tubing from the first, as a backup in case the first breaks. Braid the forelock and mane in three-five places along the neck, and weave the SPL tubing through the base of the braid to secure it to the neck. Make sure there is plenty of slack in the tubing, so that flexing and extending the neck does not place tension on it. Place a 20-gauge catheter into the tubing by backing the stylet out of the catheter just a small distance, to prevent lacerating the SPL tubing with the stylet, and inserting the catheter into the tubing up to the catheter hub. Remove the stylet. This will provide stability for the end of the tubing. Screw an injection cap onto the catheter. Use white tape to secure a tongue depressor to the braid furthest down the neck, and to secure the end of the SPL tubing, with the catheter inserted and closed off with an injection cap.

Test the patency of the SPL by injecting sterile saline or eyewash slowly through the injection port and tubing until it appears through the palpebral fissure, and runs down the face. The SPL should be checked every time medication is injected through it to ensure that the tubing has not slid through the butterfly allowing the footplate to rub on the cornea, and to ensure that medication is directed through the tubing onto the cornea, rather than being injected subconjunctivally.
Delivering SPL medications: Air or no air? The volume of medication injected into the catheter is 0.2mL of medication per dose. There are different methods of administering medications through the SPL, each with advantages and disadvantages. First, each dose of medication may be followed with 1cc of air, to clear the tubing and deliver undiluted medication to the ocular surface. The advantage of this pattern of medication administration is that it gives the eye time to absorb the first medication before it receives any additional medication, and medications do not sit in the tube where they could become inactivated by mixing with other medications, heat or light. Alternatively, each dose of medication may be delivered without flushing the tubing with air. The advantage of this method is that air isn’t blown on the corneal surface. There is some evidence that mixing medications, and that leaving medications in the tubing rather than flushing them out, may not change their efficacy (Scotty et al., 2008; Johns et al., 2010). Regardless of the method chosen, at least 5 minutes should elapse between the administration of each medication if medications are injected individually. Continuous rate infusion is another alternative (Myrna & Herring, 2006).

With a sensible patient, it is reasonable to allow small paddock turn-out even with the SPL in place, rather than restricting activity to stall rest with hand walking as is typical for more rambunctious patients, but only with willingness to accept the risk that the SPL will be damaged or dislodged and may need to be replaced (e.g., if the patient rolls and breaks the tubing, or catches it on a fence or foot.)

Eye saver masks can discourage visual inspection of the eye and the SPL, as well as provide a damp, dark, warm environment that may not be optimal for healing – so better to leave the eye uncovered. If an eye saver mask must be worn, the padding inside the cup should be changed once to twice daily to prevent moist dermatitis and irritation of the skin.

REFERENCES


EYELID LACERATION REPAIR

When repairing lacerations of the eyelid, accurate anatomical realignment of the eyelid margin is critical. Any irregularities of the eyelid margin can lead to chronic irritation of the cornea, ulceration, secondary infection and in extreme cases, loss of the globe. Two big decisions need to be made: to repair the lid standing or under general anesthesia, and to repair on the farm or refer? In many cases, the signalment of the patient (e.g., yearling) or desired outcome (e.g., perfect cosmesis for a show horse) may dictate general anesthesia and/or referral even if you think you can get it done standing on the farm. In many cases, it makes sense to discuss anesthetic options and referral, and recommend what you think is in the horse’s best interest, even if you doubt the owner will elect to do anything but have you fix the lid standing on the farm. Let the owners decline treatment options – don’t decline for them. If things don’t go the way you had hoped, you will be glad the owner declined general anesthesia or referral – but that you had at least offered.

To repair a lid laceration, ensure that you have adequate sedation and restraint. Have a plan before you start, and unless the laceration is something that a single suture can repair, incorporate two-layer closure into that plan. And take the time to prepare the skin well. The periocular skin should be prepared with betadine solution (NEVER scrub—it can cause corneal ulcers). A subcutaneous ring block can be performed to provide analgesia to the surgical site. Topical proparacaine solution is also useful to reduce corneal/conjunctival sensitivity. A povidone-iodine impregnated drape such as an Ioban drape is useful to prevent contamination of suture, but is not necessary.

Using non-absorbable suture, place a simple mattress suture to achieve closure of the tarsoconjunctival layer, with the first bite starting in the subcutaneous tissue at the apex of the laceration (furthest from the eyelid margin) and the second bite ending at the apex of the laceration. Starting away from the eyelid margin means the knot will end up away from the eyelid margin, making accurate apposition of the eyelid margin easier. If the laceration is very long, multiple sutures may be necessary, one closest to the apex of the laceration and each sequential one closer to the eyelid margin. When placing these sutures, take great care to ensure symmetry. Accurate apposition can be achieved by entering and exiting the subcutaneous tissues on each side of the incision in exactly the same. A well-placed subcutaneous suture makes accurate apposition of the eyelid margin easier, and provides a good holding layer. The conjunctiva should not be closed; it heals very rapidly without sutures. In addition, sutures through the conjunctiva will contact the cornea and result in corneal ulceration.

The next step is the figure eight, which is placed at the eyelid margin to create perfect apposition. The figure eight starts 2mm from the eyelid margin and the edge of the incision; a common mistake is to start too far away from the eyelid margin or incision. The first bite enters the eyelid skin and exits at the subcutaneous surface of the incision. The second bite enters the subcutaneous surface on the other side of the incision and exits at the meibomian glands. The third bite enters the meibomian glands on the other side of the incision and exits at the subcutaneous tissue. The final bit enters the subcutaneous tissue on the other side of the incision and exits the eyelid skin. It is absolutely essential for optimal eyelid margin alignment that perfect symmetry be maintained in this
suture pattern. Ensure that the distance between each bite and the eyelid margin and incision is perfectly symmetric. If you aren’t happy with this suture, take it out and replace it.

The remainder of the skin incision is closed in a simple interrupted pattern. The suture tails from the figure eight can be tied into the knot of the first interrupted suture in order to direct them away from the cornea.

Subcutaneous closure using simple mattress

Figure-of-eight for closing the eyelid margin

CORNEAL ULCERS

An uncomplicated corneal ulcer can usually be identified on clinical examination by application of fluorescein to the ocular surface. Fluorescein is a water-soluble (hydrophilic) molecule that is normally repelled by the hydrophobic corneal epithelium. When epithelium has been removed, as in the case of an ulcer, the hydrophilic stroma is revealed and fluorescein binds readily to it (called positive fluorescein retention or positive staining). Descemet’s membrane is hydrophobic, so if all the stroma has been lost (as in a descemetocele) then the bottom of the ulcer will not show any fluorescein retention (but the exposed stroma in the walls of the ulcer will).

Uncomplicated corneal ulcers are typically treated with a topical antibiotic to prevent infection, and topical atropine to provide cycloplegia. Remember that systemic antibiotics DO NOT achieve sufficient levels in the cornea to be effective—therefore a topical medication must be used. A broad-spectrum antibiotic is most desirable. Triple antibiotic ointment preparations (neomycin-polymyxin-bacitracin or gramicidin) are ideal. It is usually easier for an owner to get an ointment into a horse’s eye than it is to get a drop in. Atropine causes cycloplegia, or paralysis of the ciliary body, which alleviates the pain that results from the spasm of the ciliary body. Generally once daily administration or one time administration at the time of the first examination is sufficient for most patients. Atropine is generally not associated with colic or ileus in otherwise healthy adult horses,
although young foals do seem susceptible to ileus associated with atropine. Atropine should be used cautiously in young patients (once daily or less). Since atropine also causes mydriasis, horses treated with atropine may exhibit some photophobia. If tolerated, a fly mask could be placed on horses with exposure to direct sunlight while they are being treated with atropine. The effects of atropine are prolonged in a normal eye; a normal horse eye can remain dilated for 2-4 weeks after a single dose of atropine. Because atropine causes decreased accommodation via its mechanism of cycloplegia, horses also presumably have a decreased ability to focus while being treated with the drug. Riders of performance horses must exercise caution when riding a horse being treated with atropine, and avoiding tasks that involve evaluating depth of field is advisable (ie. jumping). While atropine does provide some analgesia, superficial ulcers are very painful (remember that the superficial cornea is more densely innervated than the deeper cornea). A short course (e.g., 3-5 days) of a systemic non-steroidal anti-inflammatory (NSAID) can be used to provide additional analgesia.

A horse with a simple corneal ulcer should be rechecked in 3-5 days to ensure healing is progressing as expected or sooner if any signs of increased blepharospasm, discharge, redness or cloudiness of the corneal surface is noted.

Complicated corneal ulcers are ulcers that involve stromal loss, may be infected, may have factors complicating healing such as facial nerve paralysis or eyelid neoplasia, and do not heal in an appropriate amount of time (i.e., 7-10 days). These ulcers require recognition and correction of the complicating factor before they will heal. Complicated ulcers are defined by the following criteria:

1. **Deep/stromal loss**—anytime an ulcer involves loss of both epithelium and stroma, it becomes complicated to heal. While epithelium is highly mitotically active, stroma is largely acellular collagen fibers with few keratocytes. When the stroma is wounded, the process of activating keratocytes into fibroblasts that synthesize and replace the collagen is lengthy and prolongs the course of wound healing. Wounds that involve loss of stroma are slower to heal and more likely to develop secondary complications like infection or malacia. An ulcer that has lost all stroma down to the level of Descemet’s membrane is termed a descemetocele. Remember that all that stands between the inside the eye and the outside world in a descemetocele is a single layer of endothelium and its basement membrane!
2. **Infection/melting**—Infection is visible in the cornea as yellow/white/tan cellular infiltrate within the stroma. Infected ulcers also tend to be more painful because of the greater involvement of the stroma. The presence of infection can be confirmed with cytology and culture/sensitivity. Keratomalacia, or melting of the cornea is the dissolving of the stromal collagen due to the action of collagenase and protease enzymes. There are two major sources of collagenase and protease: infectious organisms (bacteria, fungi) and white blood cells (especially neutrophils). Corneal melting can lead to corneal perforation if not treated appropriately. Melting tends to be associated with infection in the majority of cases, but sterile ulcers can also melt.

3. **Do not heal in an appropriate amount of time**—Any corneal ulcer that has not healed within 7 days should be considered a complicated ulcer. In order to determine why the ulcer is not healing, a careful examination must be performed in order to rule out stromal loss, infection or other complicating factors. The most common reason for delayed healing in horses is infection.

4. **Complicating factors are present**—Complicating factors describe a variety of causes of corneal ulceration that must be addressed before corneal wound healing can occur. Examples of complicating factors include infection, facial nerve paralysis leading to an inability to blink, entropion, eyelid tumors, ectopic cilia, glaucoma, corneal denervation/CN V deficit and systemic immunocompromise (Cushings disease/equine metabolic syndrome). If these underlying factors are not addressed, the ulcer will not heal. Once the factor is resolved, the ulcer should heal without further inhibition.

Making the diagnosis of a complicated corneal ulcer should start with a complete ophthalmic examination. Note that in cases of extreme stromal loss (> 90%), extreme caution should be taken in handling the lids and globe. Sedation and an auriculopalpebral nerve block is particularly important if the cornea is fragile to prevent inadvertent rupture of the globe. If corneal cultures are to be obtained, they should be obtained prior to instilling any drops into the eye, including proparacaine or fluorescein as these may inhibit microbial growth. Cytology should also be obtained prior to instilling fluorescein if possible. Cytology and culture/sensitivity (for both bacteria and fungus) should be considered mandatory diagnostic tests in all cases of complicated corneal ulceration, particularly those with stromal loss, infection or melting. The results of
cytologic evaluation will guide your initial choice of therapy, and culture/sensitivity will confirm or alter those choices.

Treatment of the complicated corneal ulcer is summarized as follows:

1. **Stromal loss**—If there is > 50% stromal loss, the ideal treatment is surgical stabilization, such as a conjunctival or corneal graft. In these cases, the cornea is at risk of rupture with subsequent loss of vision from retinal detachment or chronic uveitis and cataract formation. These patients should be referred to a veterinary ophthalmologist for evaluation. If referral is not an option, manage as an infected/melting ulcer. In the case of corneal laceration with iris prolapse or descemetocele, referral should be strongly encouraged.

2. **Infection/melting**—Cytology should guide initial antibiotic choices when possible. Most infected/melting ulcers will require frequent treatment of a painful eye (Clode, 2010). Placement of a sub-palpebral lavage (SPL) tube facilitates treatment and makes treatment less uncomfortable for the patient. Only solutions (not ointments) can be administered via SPL. The two major categories of common infectious organisms are bacteria and fungi. If a mixed population of bacteria are observed on cytology, a fluoroquinolone such as ofloxacin 0.3% or ciprofloxacin 0.3% is a reasonable starting place. An aminoglycoside such as tobramycin may be added if gram negative bacteria are observed, or a cephalosporin or triple antibiotic may be added if gram positive bacteria are observed. Antibiotic therapy should begin q2-4 hours and then decrease as the infection becomes controlled. In regions where fungal keratitis is common, even if no fungal hyphae are observed on cytology, anti-fungal therapy is indicated. Commonly used antifungals include voriconazole 1%, itraconazole 1%, and natamycin 5%. Antifungals are often chosen based on geographic trends in susceptibility, because antifungal susceptibility testing is costly, and takes time to return results. Anti-fungal therapy may be less frequent initially, to reduce uveitis associated with fungal death, then increased as needed. Because fungi are more resistant to drug therapy than bacteria, treatment of fungal keratitis in the horse is often prolonged (several weeks to several months). The melting component must be addressed with anti-collagenase and anti-protease therapy (Ollivier et al, 2003). Autologous serum (serum harvested from the patient) is a highly effective anti-collagenase/protease. Serum should be stored aseptically in the refrigerator and replaced every 5-7 days. EDTA, topical tetracyclines, systemic tetracyclines and N-acetylcysteine are other anti-collagenase/proteases that can be utilized in addition to autologous serum. EDTA solution can be prepared by filling a purple top EDTA blood tube half way full with sterile saline. The resultant solution can be administered directly to the ocular surface. The frequency of administration depends on the severity of the disease, with q1-2h administration recommended for the most severely affected cases. Referral is appropriate for patients with infected or melting corneal ulcers. The advantages of referral include access to diagnostics (ie. cytology), hospitalization (which allows frequent treatment of severe corneal disease) and prompt surgical intervention where necessary. Sub-palpebral lavage systems can be placed and managed on the farm with a committed and educated owner. Analgesia must be addressed in patients with a infected or melting ulcer. Oral NSAIDS and topical atropine are indicated in most patients. As the use of oral NSAIDS will be chronic in most cases, appropriate monitoring of total protein, renal and other gastrointestinal parameters is warranted.
3. Not healing in appropriate amount of time—If a corneal ulcer is not healed within 7 days, it is considered complicated. It is important to consider why the ulcer isn’t healing and look for evidence of stromal loss, infection/melting or other complicating factors. Since infection is the most common cause of delayed healing in the equine cornea ulcer, it is particularly important to test for infection via cytology and culture prior to suspecting an indolent ulcer (Michau et al, 2003).

REFERENCES


3. Diagnostic Approach to the Cloudy Eye: What to Do if the Eye is Blue (or White or Yellow)

The cloudy eye can prove a diagnostic challenge. A complete ocular examination, including fluorescein stain, provides the basis for identifying features that can help inform the diagnosis. Categorizing the eye on two features can help: Is the eye painful, or not? And, is there a corneal ulcer present (i.e., is there fluorescein uptake), or not? The following nonulcerative ocular diseases often present as a cloudy eye.

**STROMAL ABSCESS**

Stromal abscesses occur more frequently in horses than any other species. They appear clinically as yellow-tan circular to multifocal stromal lesions associated with intense ocular pain, blepharospasm, tearing, variable corneal vascularization and secondary uveitis. The hallmark of a corneal stromal abscess is ocular pain that is disproportionate to the apparent severity of the lesion.

Stromal abscesses can be frustrating to diagnose, as the abscess may be located beneath intact epithelium and thus fluorescein negative. When uveitis is severe, corneal edema and vascularization may preclude view of the abscess. Extreme caution must be exercised when treating a corneal opacity that is fluorescein-negative (i.e., there is no corneal ulcer present) with a topical steroid, as steroids can exacerbate an abscess.

Even when a stromal abscess is associated with a corneal ulcer, they cannot be lanced and drained as a hoof abscess or subcutaneous abscess can since the abscess material is cellular and not liquefied. This makes obtaining abscess material for cytology and culture challenging. In most cases, it is safest to presume that a stromal abscess contains both bacterial and fungal organisms and to treat accordingly. Treatment for stromal abscesses can be medical or surgical.

Medical therapy is as for an infected ulcer. Debridement of the overlying epithelium may improve drug penetration, although this creates an open wound which is susceptible to infection, so this is not generally recommended. Drug penetration is likely better through the inflamed cornea than the normal cornea. Medical therapy is prolonged in many cases, from several weeks to several months. Subpalpebral lavage systems are very useful in treating stromal abscesses, both due to prolonged treatment, and severe pain.

Medical treatment of stromal abscesses involves topical antibiotics (usually a fluoroquinolone solution, such as ofloxacin or levofloxacin, since they are both broad-spectrum and possess excellent ability to penetrate the cornea) and topical antifungals (which vary by region, and include voriconazole, itraconazole, and natamycin). Stromal abscesses can be associated with severe secondary uveitis, which should be treated with topical atropine, systemic NSAIDs and topical NSAIDs. When medically managing stromal abscesses, the end-goal of treatment is a visual, comfortable eye.
Generally the abscess will heal by vascularization, thus the use of topical/systemic anti-inflammatories is a balance between inhibiting vascularization of the cornea and control of vision-threatening uveitis. As the abscess vascularizes, systemic antibiotics and antifungals may be useful. Oral sulfas are the antibiotic of choice as they are inexpensive, relatively broad-spectrum and easy to administer. Fluconazole is often chosen as a systemic antifungal (loading dose 14mg/kg PO once, then 5mg/kg PO q24h), although its efficacy against Aspergillus species is limited. Treatment should be continued until the abscess has vascularized and the vessels are regressing, leaving behind a grey area of fibrosis.

Surgical therapy includes excision of the abscessed stroma with supportive grafting procedures to return the cornea to normal tectonic strength. Referral for surgical therapy by a veterinary ophthalmologist is strongly recommended.

Surgical procedures include penetrating keratoplasty (PK) for full thickness stromal abscesses, or partial thickness grafts such as the posterior lamellar keratoplasty (PLK) or deep lamellar endothelial keratoplasty (DLEK). PLK and DLEK are indicated for deep stromal abscesses with a clear anterior stroma (Brooks et al., 2008). Surgical therapy combined with medical therapy is typically associated with a shorter duration of therapy and faster recovery than treatment with medical therapy alone, although scar formation may occur.
REFERENCES


IMMUNE-MEDIATED KERATITIS

Immune-mediated keratitis (IMK) has been described as a chronic (i.e., greater than three months in duration), nonulcerative corneal opacity that is not believed to be caused by an infectious agent, and typically responds to topical immunosuppressive drugs such as prednisolone acetate, dexamethasone, cyclosporine, or tacrolimus (Gilger et al., 2005). Three types have been described, based on the depth of the stromal infiltrated:

1. Superficial: infiltrate, diffuse vascularization, response to medical therapy or keratectomy
2. Midstromal: infiltrate, mild focal edema, vascularization, response to cyclosporine
3. Endothelial: infiltrate, diffuse edema, poorest prognosis

IMK is not typically associated with uveitis or with pain. Medical therapy tends to be constant, and in some cases, surgery can be curative.

EOSINOPHILIC KERATITIS

Eosinophilic keratitis is an inflammatory condition of the cornea characterized initially by severe pain and limbal corneal ulcers, often accompanied by a caseous discharge and severe chemosis and conjunctival hyperemia. The disease has a seasonal occurrence in the summer, likely associated with an environmental stimulus or insect vector. The presence of eosinophils on cytology is diagnostic. Treatment with topical steroids is often associated with secondary fungal infection. Systemic steroids and antihistamines may reduce disease severity. Treatment is
typically prolonged. Recurrence from year to year in the same patient is reported. Treatment with the antihistamine cetirizine may decrease the likelihood of recurrence.

REFERENCES


EQUINE RECURRENT UVEITIS

Equine Recurrent Uveitis (ERU), has been described as the leading cause of blindness in horses. Alternate names include moon blindness and periodic ophthalmia. Uveitis starts as blood-ocular barrier compromise, such that blood vessels of the iris, ciliary body and choroid become “leaky”, allowing cells and inflammatory cytokines to enter the eye. Infectious agents may initiate the initial flareup of uveitis but immune response shifts between different autoantigens may be responsible for recurrent episodes. Corneal, lens and retinal autoantigens have been identified in the equine eye that are believed to be targeted by the immune system in horses with ERU; these self-antigens perpetuate the disease. While Leptospirosis has been implicated in the initiation of ERU, the continued presence of the Leptospira organism in the aqueous or vitreous humors does not appear to play a direct role in the pathogenesis of ERU (Gilger et al., 2008).

Cyclosporine A implants have been developed to decrease the frequency and severity of flareups of ERU. Most horses with CsA implants have less inflammation and fewer attacks postoperatively (Gilger et al., 2010).

Standard treatment of ERU flareups remains topical corticosteroids and nonsteroidal anti-inflammatory agents, topical atropine, and systemic anti-inflammatories (both corticosteroids and NSAIDs). There are risks and complications associated with long term use of any of these drugs.
REFERENCES


EQUINE GLAUCOMA

Glaucoma is a disease characterized by elevation of intraocular pressure (IOP) that is incompatible with health of the optic nerve. In horses, glaucoma is usually secondary to uveitis. Clinical signs include mydriasis, cornea edema, scleral injection, ciliary flush, and in chronic cases, buphthalmos. Haab’s striae, which represent breaks in Descemet’s membrane, may be associated with glaucoma, but can also be seen as inflammatory lesions. Glaucoma is diagnosed based on clinical signs and measurement of IOP. Several different types of tonometer are commercially available and lend themselves well to field use.

Tonometry can easily be performed in the equine eye to assess intraocular pressure (IOP). It is essential to ensure the head is level with the heart prior to performing tonometry in order to minimize the effects of changes in head position on intraocular pressure. Intraocular pressure can more than double in a normal, sedated horse simply by placing the head at the level of the knees! (Komaramy & Garg, 2006). Take great care to avoid inadvertent pressure on the globe with your fingers. Stabilizing the eyelid against the orbital rim, using sedation and performing an auriculopalpebral block will help avoid artificially elevated IOP measurements. Either an appplanation tonometer (most commonly the “Tonopen”) or rebound tonometer (most commonly the “Tonovet”) can be used to measure IOP in horses. Both devices are accurate for clinical use (Knollinger & La Croix, 2005).
Glaucoma can be classified as primary, resulting from anatomic abnormalities associated with the iridocorneal angle, or secondary to other ocular disease such as uveitis, lens luxation or intraocular neoplasia. Primary glaucoma is not well characterized in the horse.

Therapy for glaucoma can be divided into two general categories: drugs that decrease aqueous production, such as beta blockers and carbonic anhydrase inhibitors, and drugs that increase aqueous outflow, such as prostaglandin analogs. Another way of categorizing glaucoma medications would be based on their function, as rescue versus maintenance drugs. Some drugs, like the prostaglandin analogs (e.g., Latanoprost®, or latanoprost) serve both rescue and maintenance functions. Unfortunately, the prostaglandin analogs, which have proven to control IOP well in other species, do not decrease IOP in horses. The two drugs most helpful in decreasing IOP in horses with glaucoma are timolol and dorzolamide, which are available as a combination product called Cosopt®.

As with medical therapy, surgical treatments for glaucoma can be classified based on their mechanism of action as either decreasing aqueous production (e.g., cyclodestructive procedures, which damage the ciliary body) or increasing aqueous outflow (e.g., anterior chamber shunts). Diode laser transcleral cyclophotocoagulation (TSCP) can provide long term control of IOP in horses with glaucoma, but typically does not eliminate the need for long term topical treatment (Annear et al., 2010). TSCP can often be performed under standing sedation rather than general anesthesia. Horses undergoing TSCP typically have a three week period in which IOP spikes in association with laser-induced uveitis, but then settles down to a stable postoperative level.

Endocyclophotocoagulation (ECP) and gonioimplant placement have become increasingly commonly performed by veterinary ophthalmologists treating canine glaucoma patients, but neither of these surgical therapies have yet achieved success with equine glaucoma patients.

REFERENCES


4. **Ocular Prepurchase Examination: No Eye, No Horse**

The ocular examination is an important part of the pre-purchase examination for any horse. While some horses may be capable of doing their jobs with impaired vision or even blind, ocular disease that affects or has the potential to affect vision can stop a potential buyer in their tracks, before the musculoskeletal soundness of the horse has even been addressed. So just how common is ocular disease? What is involved in performing a complete ocular examination? And what ocular conditions might be picked up on pre-purchase examination?

**Incidence of Ocular Disease**

In one study reporting ophthalmic examination findings in over 200 Thoroughbred racehorses in Australia (Hurn & Turner, 2006), potential vision-threatening ocular disease was present in 7% of the horses, and non-vision threatening ocular disease was present in 57%. Vision-threatening eye disease included complete cataracts, large peripapillary ‘butterfly’ lesions and optic nerve atrophy. Non-vision threatening ocular disease included lower eyelid scars, periorcular fibropapillomatous disease (i.e., sarcoid), third eyelid squamous cell carcinoma, corneal scars, corneal band opacity, anterior iris synechia, incipient or immature cataracts, and peripapillary focal inactive ‘bullet hole’ chorioretinal lesions (of a number low enough to be deemed insignificant to affect vision). This last finding occurred in over half of the horses in this study! Unusual variations of normal ocular anatomy and colobomata were recorded in 5% of the horses, including hypoplastic or cystic corpora nigra, hyaloid remnant, lens coloboma and retinal coloboma. The take-home message from this report is that if you are doing pre-purchase examinations, you will see horses with ocular abnormalities, and your clients will look to you to diagnose and interpret these findings, and make recommendations regarding the disposition of the horse involved.
PERFORMING A PREPURCHASE EXAMINATION

Examination of the equine eye may be greatly facilitated by sedation, depending on the temperament and ocular comfort of the patient. It can be tempting to skip sedation to save time and money, and to avoid interfering with the remainder of the prepurchase, but if the ocular examination can’t be performed adequately without sedation, it is well worth it to just sedate the patient and do a good job. A short-acting injectable alpha-2 agonist such as xylazine is ideal for ophthalmic examination. Injectable opioids such as butorphanol should be avoided as they are associated with increased spontaneous head movement. Administration of topical anesthetic agents, such as proparacaine hydrochloride, may also facilitate examination of a painful eye. If squinting interferes with the ocular exam, the auriculopalpebral nerve, a branch of cranial nerve VII (facial nerve) can be blocked using 1-2mL of local anesthetic such as 2% lidocaine or 2% mepivicaine deposited subcutaneously where the nerve is easily palpated over the dorsal border of the zygomatic arch.

A Finoff transilluminator is the instrument of choice for beginning an ocular exam. A penlight may not be bright enough to elicit pupillary light reflexes or illuminate the anterior chamber, although a MagLight may get the job done. Even when a location with bright ambient lighting is the only option for performing the ocular exam, a bright focal light source can improve view of the eye. To perform a complete ocular exam, evaluate each of these components:

FUNCTIONAL VISION. Observe the horse, both in a familiar environment (such as a stall) and in a novel environment (if possible). If the visual status of the horse is unclear, observing the horse in a maze test in both dim and bright light conditions can be helpful. A simple maze can be constructed in the barn aisle using objects on the ground such as poles or brooms that will not result in injury if the horse takes a misguided step.

FACIAL AND GLOBE SYMMETRY, AND OCULAR COMFORT. Observe the horse from the front and from the side. Asymmetry in the angle of the eyelashes, with the lashes pointing down in one eye, can indicate pain or light sensitivity. Observe the face for any sign of ocular discharge, either wet or dried on the face. Observe the globes for symmetry in size. A globe that appears smaller than the other can be displaying early signs of phthisis bulbi (end-stage eye) or enophthalmos (normal size but recessed into the orbit) associated with pain; a globe that appears larger may be exophthalmic (normal size but protruding) or buphthalmic (enlarged due to increased intraocular pressure and glaucoma).

VISION RESPONSES AND LIGHT REFLEXES. A menace response (which is NOT a reflex!) can be evaluated by bringing a closed hand towards the eye, trying to avoid the creation of unnecessary air currents or touching any long vibrissae that may be present. The menace test should be performed in five quadrants, dorsal, ventral, temporal, nasal and axial, and the opposite eye should be covered to prevent false positive responses. The palpebral reflex is tested by gently touching the medial and lateral canthus. This touch should elicit a brisk blink. A dazzle reflex is tested by shining a bright focal light into the eye. This should elicit a brisk blink or avoidance response. To test pupillary light reflexes (PLRs), first assess pupil size prior to light stimulation, taking into account the ambient lighting conditions and what pupil size is appropriate for the conditions (smaller in bright light, larger in dim light). Next, illuminate one pupil while observing
the amplitude and speed of the PLR (direct PLR). The observer can ask for an assistant to look at the PLR of the contralateral eye or can simply move very quickly to the contralateral eye to observe the PLR themselves (consensual PLR).

ANTERIOR SEGMENT. Carefully observe the adnexa, including the eyelid skin and eyelid margin. The eyelids should be gently everted to examine the bulbar and palpebral conjunctiva. Gentle pressure will retropulse the globe, allowing exposure of the third eyelid. Any defects of the eyelid margin, masses or ulcerative lesions should be noted. The cornea should be inspected for any opacities or changes in thickness. Fluorescein stain should be applied to evaluate the integrity of the corneal epithelium. The anterior chamber should be examined for any opacities, exudates or masses. The iris should be examined for any changes in the color or texture of the iris and corpora nigra or masses of the iris.

LENS AND FUNDUS. Evaluation of structures posterior to the iris cannot be done thoroughly without pharmacologic dilation (e.g., with tropicamide). If dilation is declined, either due to time or performance constraints, this should be noted clearly in the exam summary with a statement making it clear that lens and posterior segment examination was incomplete (e.g., “Structures posterior to the iris could not be examined completely due to miosis, but no abnormalities were found in the lens or fundus through a miotic pupil”). Any opacities or changes in shape or in position of the lens should be described as precisely as possible. The color and character of the tapetal reflection and vitreous should be evaluated. The retina can be examined using a variety of instruments, including a direct ophthalmoscope, a Panoptic ophthalmoscope and an indirect hand lens. Regardless of the instrument, the tapetal color and reflectivity, optic nerve head shape and size, retinal blood vessel shape, size and number, and non-tapetal retina color and reflectivity should be carefully observed.

OCULAR DISEASE OF CONCERN ON PREPURCHASE EXAMINATION

Fundic lesions. Most fundic lesions in horses occur near the optic nerve head, and involve either depigmentations or hyperpigmentation (Cutler et al., 2000). In color-dilute horses such as those with a gray or white coat, choroidal vasculature which is normally obscured by the pigmented nontapetal fundus is visible, and may be mistaken for retinal hemorrhage.

Cataract. A cataract is an opacity in the lens of the eye. Cataracts may be categorized based on location (capsular, subcapsular, cortical, nuclear, equatorial), etiology (inherited, traumatic,
metabolic, uveitic), and by stage of progression (incipient, immature, mature, and hypermature). Any cataract is a potential visual impairment. The relationship between vision and performance in horses has not been clearly elucidated, and therefore risks associated with various degrees of visual impairment in horses with cataracts, as well as with other vision-impairing ocular diseases, remain unclear.

Surgical removal is the only treatment for cataracts. To be considered a good candidate for cataract surgery, the horse must be a good candidate for general anesthesia. In addition to preanesthetic evaluation, horses that are being considered as candidates for cataract surgery typically undergo ocular ultrasound, to evaluate each affected eye for presence of a retinal detachment, and electroretinogram (or ERG), to test retinal function. The idea behind the ocular diagnostics is to minimize the chance as much as possible of operating on a horse whose vision will not be improved by cataract surgery (e.g., a horse who already has a retinal detachment, or retinal degeneration). As in other species, artificial lenses called IOLs (i.e., intraocular lenses) are placed intraoperatively if possible, to return the horse to vision that is as close to perfect as possible (McMullen & Utter, 2010).

Cataracts in horses often develop secondary to ERU. Horses with cataracts secondary to ERU may still be viable candidates for cataract surgery, as long as the owner accepts the increased risk of complications and is committed to vigilant postoperative monitoring and close compliance with follow-up recommendations.

REFERENCES

